

ROGO 211.3-NDH

Claim 13, line 1: change "Composition" to -- Intravenous composition --.

Claims 14, 15, 16, 17 and 18, line 1 of each: after "The" add -- intravenous --.

REMARKS

Entry of the amendment is requested. Claims 1-10 and 13-18 will be before the Examiner. Claim 11 is incorporated into claim 1. Claims 13-18 are amended to parallel claim 1.

Attached hereto is a definition of the term "endotoxemia", from Stedman's Medical Dictionary:

"The presence in the blood of endotoxins which, if derived from Gram negative, rod shaped bacteria, may cause a generalized Schwarzman phenomenon with shock.

(emphasis added). Endotoxemia, then, is a condition characterized by toxins in the blood. Applicants have used this term in the standard, art recognized way. The prior art relied upon by the Examiner has not.

The Examiner has relied on Lichtenberger in combination with Cahill to find all claims obvious. Applicants have considered the rejection carefully, and have studied the art in detail. They now traverse the rejection, for reasons which follow.

The sole reference to endotoxins in Lichtenberger is at column 3, line 25, referring to a putative toxin in the lumen of the lungs. At column 11, lines 28-31, Lichtenberger describes

ROGO 211.3-NDH

"endotracheal" administration as being the preferred mode of administration. No other modalities are disclosed. While Lichtenberger does disclose treatment of, e.g., ulcers, these conditions are not alleged to be associated with endotoxins, and in any event the administration is intragastrically. See column 26, line 28. Note that the endotoxins of Lichtenberger are not associated with classical endotoxemia.

Cahill does not correct these deficiencies. This reference deals with jaundice and renal failure. The authors allegedly address the problem via oral administration of sodium deoxycholate. See page 467, second column, first five lines of "Bill salts". This approach might be useful in preventing endotoxins from entering the blood, but once the endotoxins are in the blood - and endotoxemia occurs - administration in the manner proposed by Cahill simply will not work. There is no evidence that the cholates are transported into the blood.

Thus, the prior art does not fairly teach treatment of endotoxemia, because the field recognizes this as a blood condition - not a pulmonary or renal one. Further, the art teaches intragastric, endotracheal, and oral administration of different portions of what is claimed. There is no suggestion to administer the drug intravenously, nor is there a teaching of endotoxemia as the art knows it, nor is there a suggestion to combine the different components as is claimed. Thus, one cannot conclude that claims 1-10 and 13-18 are obvious. The rejection should be withdrawn, and the application passed to allowance.

ROGO 211.3-NDH

A prompt notice to that end is urged.

Respectfully submitted,

FELFE & LYNCH

By


Norman D. Hanson
Reg. No. 30,946

805 Third Avenue
New York, New York 10022
(212) 688-9200

ILLUSTRATED
Stedman's
MEDICAL
DICTIONARY

24TH EDITION



WILLIAMS & WILKINS
Baltimore/London

BEST AVAILABLE COPY

endothelia

466

energy

energy

tendon.

endothelia (en'do-thé'li-ah). Plural of **endothelium**.
endothelial (en'do-thé'li-al). Relating to the **endothelium**.
endotheliocyte (en'do-thé'li-o-sit). **Endothelial leukocyte**.
endothelioid (en'do-thé'li-oyd). Resembling **endothelium**.
endothelioma (en'do-thé'li-o'mah). A generic term for a group of neoplasms derived from the **endothelial tissue** of blood vessels or lymphatic channels; *e.* may be benign or malignant.

endotheliosis (en'do-thé'li-o'sis). Proliferation of **endothelium**.

endothelium, pl. **endothelia** (en'do-thé'li-um, -li-ab) [*endo-* + G. *thélē*, nipple]. A layer of flat cells lining especially blood and lymphatic vessels and the heart.

e. of the anterior chamber, *e.* cameræ anterioris.

e. cameræ anterio'ris [NA]. **endothelium** of the anterior chamber; a single layer of large, squamous cells that covers the posterior surface of the cornea.

endotheliolysis. Denoting a chemical reaction during the progress of which there is absorption of heat; *cf.* **endothermic**.

endothrix [*endo-* + G. *thérē*, hair]. A trichophyton (notably *Trichophyton violaceum* and *T. tonsurans*) whose spores and, occasionally, mycelia characteristically invade the interior of the hair shaft; there is no conspicuous external sheath of spores, as there is with **ectothrix**.

endothyroidopexy (en'do-thi'roy'do-pek-si). **Endothyropexy**.

endothyropexy (en'do-thi'ro-pek-si) [*endo-* + thyroid + G. *péxis* a fixing]. **Endothyroidopexy**; operative dislocation of the thyroid gland and its fixation in the side of the neck.

endotoxemia (en'do-tox'é-mi-ah). The presence in the blood of endotoxins, which, if derived from Gram-negative, rod-shaped bacteria, may cause a generalized Schwartzman phenomenon with shock. **Gram-negative**.

endotoxicosis (en'do-tox'é-ko'sis). Poisoning by an endotoxin.

endotoxin. Intracellular toxin. 1. A bacterial toxin not freely liberated into the surrounding medium, in contrast to exotoxin. 2. The complex phospholipid-polysaccharide macromolecules which form an integral part of the cell wall of a variety of relatively avirulent as well as virulent strains of Gram-negative bacteria including the *enterobacteriæ*, *vibrion*, *brucellæ*, and *neisseriæ*; they are released only when the cell wall is disturbed, are relatively heat-stable, are less potent than most exotoxins, and are less specific; they do not form toxoids; when injected in sufficient quantities, they cause a state of shock accompanied by severe diarrhea, and, in smaller doses, fever and leukopenia followed by leukocytosis; they have the capacity of eliciting the Schwartzman and the *Sanarelli-Schwartzman* phenomena.

endotracheal (en'do-trá'ke-al). Within the trachea.

endotrachelitis (en'do-trák'ké-lit'is). **Endocervicitis**.

endovaccination (en'do-vak'si-na'shun). Oral administration of vaccines.

endovascularis (en'do-vás'ku-lá'tis). Endangiitis.

endovenous (en'do-ve'núüs). Intravenous.

end-piece. The terminal part of the tail of a spermatozoon consisting of the axoneme and the flagellar membrane.

end'plate, **end-plate**. The ending of a motor nerve fiber in relation to a skeletal muscle fiber.

motor e., sole-plate ending; the large and complex end-formation by which the axon of a motor neuron establishes synaptic contact with a striated muscle fiber (cell); several terminal branches of a motor axon end in irregular, club-shaped synaptic end-formation which are bedded in a single trough-like depression of the muscle fiber's surface; the postsynaptic membrane, the sarcolemma that forms the bottom of the trough, is greatly increased in surface area by deep infoldings protruding into the underlying cytoplasm of the muscle fiber; the subsynaptic interval between the plasma membrane of the axon terminals and the sarcolemma is filled with an amorphous substance; the trough is closed off toward the surface by the Schwann sheath which peels away from the axons as the latter cover the trough, and thus forms a lid

over the trough; the slight bulge of this closure plate corresponds to Doyère's eminence.

end-tidal. At the end of a normal expiration.

endyma (en'di-mah) [G. *éndyma*]. **Ependyma**.

E.N.E. Abbreviation for ethylmorphine.

-ene. A suffix applied to a chemical name indicating the presence of a carbon-carbon double bond; *e.g.* propene (unsaturated propane, $\text{CH}_3 - \text{CH} = \text{CH}_2$).

enediol (en-di'ol). A substance formed by proton migration from a $-\text{CHOH}$ group *a.* to an aldehyde or a ketone, usually induced by alkali, giving rise to doubly bonded carbon atoms (the *ene* group) each bearing a $-\text{CHOH}$ group (*a diol*); a special case of cyclization; $-\text{CH}(\text{OH}) - \text{CO} - \text{C}(\text{OH}) = \text{C}(\text{OH}) -$.

enema (en'é-mah) [G.]. A rectal injection for the purpose of clearing out the bowel, or administering drugs or food.

enamptic e., an *e.* of a pint of lukewarm water with one-half teaspoonful of table salt.

barium e., contrast *e.*; administration of barium, a radioopaque medium, for x-ray study of the lower intestinal tract.

blind e., the introduction into the rectum of a rubber tube to facilitate the expulsion of flatus.

contrast e., barium *e.*

double contrast e., after evacuation of a barium *e.* and injection of air into the rectum, x-ray study will show finer details of mucosa of the rectum and colon.

flatus e., an *e.* of magnesium sulfate in glycerin and warm water.

high e., enecyclosis; an *e.* instilled high up into the colon.

nutrient e., a rectal injection of predigested food.

oil retention e., mineral oil introduced at low pressure and retained for several hours before expelling, for the purpose of softening feces.

soapsuds e., an *e.* of shredded or powdered soap in warm water.

turpentine e., an *e.* of turpentine and olive oil in soapuds.

enem'ator. An appliance for use in giving an **enema**.

enemi'asis. The use of enemas.

energetics (en'er-jé-tiks). The study of the energy changes involved in physical and chemical changes.

energom'eter [G. *energeia* energy, + *metron* measure]. An apparatus for measuring blood pressure.

energy (en'er-jé) [G. *energeia* fr. *en*, in, + *ergon* work].

Dynamic forces; the exertion of power; the capacity to do work, taking the forms of kinetic *e.*, potential *e.*, chemical *e.*, electrical *e.*, surface *e.*, etc.

e. of activation, usually expressed of *e.* that must be added to that already possessed by a molecule or molecules in order to initiate a reaction; usually expressed in the Arrhenius equation relating a velocity constant to absolute temperature.

binding e., the *e.* that would be released if a particular atomic nucleus were formed through the combination of individual protons and neutrons.

chemical e., *e.* liberated by a chemical reaction or absorbed in the formation of a chemical compound.

free e., a thermodynamic function symbolized as *F* or *G* (Gibbs' free *e.*); defined as $H - TS$, where *H* is the enthalpy of a system, *T* the absolute temperature, and *S* the entropy; chemical reactions proceed spontaneously in the direction that involves a net decrease in the free *e.* of the system.

Gibbe's free e., see free *e.*

kinetic e., the *e.* of motion.

latent e., potential *e.*

nerve e., potential *e.*

nervous e., neuricity.

nuclear e., *e.* given off in the course of nuclear reaction or stored in the formation of an atomic nucleus.

nutritional e., trophodynamics.

e. of position, potential *e.*

potential e., latent or nerve *e.*; *e.* of position; the *e.* existing in a body by virtue of its position or state of existence, which is not being exerted at the time.

psychic e., psychic force; in psychoanalysis, a hypothetical mental force regarded as analogous to the physical concept of *e.*; *e.* enabling and vitalizing an individual's psychological activity. See also libido.

radiant e., the *e.* emitted of radiation.

solar e., the *e.* of sun; total *e.*, the sum of all emanations (em'er-va'shu-ate, fr. *e.* priv. + *em*- weakening).

enflurane. 2-Chloro-1-ether; a potent volatile nonflammable and nonexplosive.

ENG. Abbreviation for engagement (en'gaj'mént).

engastrus (en-gas'tri-u'sual). Conjoined twins in wholly or partly within (autozygous).

Engel, Rudolph C., Als. *E.*'s alkalimetry.

Engelmann, Guido, C. disease.

Engelmann, Theodor 1909. See *E.*'s basal *ku*-engine (en'jin). An app. mechanical energy or *ku*-dental *e.*, the motive *pc* causes the instrument *t* turbine but often a *fric* with a *belt* drive.

en'gine'ing. The practical, chemical, and mathematical biomedical *e.*, the app. solutions to biomedical laboratory of engineers.

dental e., the application genetic *e.*, modification heredity by manipulation

Engleb, Josef. Vienna.

englobe (en-glôb). To take the ingestion of bacteria phagocytes.

englob'e'ment. The body, such as a leukocyte engorged (en-gorj'd) [O narrow passage, fr. L. *füll*; distended with fluid engorgement (en-gorj'm) or material. See also *en'grain* [G. *en* in, + *gráfein* (g'f), a phys. on the protoplasm of a stimuli.

engraphia (en-graf'í-ah).

en grape (ahn-grap'). Denoting the microconidium of certain enhance'ment. 1. The *angy*, the prolongation of an opposing process.

contrast e., the intra-soluble iodinated contrast number of the vascular (particularly in the brain) the interstitium.

immunological e., the having an opposing effect tissue transplantation (allograft (homograft) in previous transplant can animal with dead tissue dies of the same kind.

en'grain (en'grain). Enkephalin (en-kef'ál-in).

en'grap'thaphy. Enceps